Brief Summary Text (150):
Furthermore, the liposomes of the invention can be used prophylactically and therapeutically with different eye diseases, such as allergically or virally caused inflammations, irritations due to lacking or physiologically unfavorably composed lacrimal fluid and damage caused by chemical or physical action.

Brief Summary Text (151):
Many inflammatory eye diseases are triggered by allergens or viruses and lead, enhanced by bacterial superinfections, to impairments which will often be permanent. How sensitive the eye tissues are becomes already apparent from the fact that many general disorders (such as a cold) lead to eye diseases (such as conjunctivitis). The problems arising from present treatments of allergic and viral diseases have already been described in sections I and II, but are even more pronounced with eye treatments. For instance, the corticosteroids which are often applied in the case of inflammatory processes must not be used in case of damage to the epithelium of the cornea, as this might otherwise lead to a rapid progressive ulceration and possible perforation with loss of eye. Some antiallergics lead to a reduction of the lacrimal fluid, thereby creating new problems. The virostatics presently approved on the eye (e.g. aciclovir) can only be applied in case of emergency due to their strong side effects. The irritations which can often be observed and are caused by lacking or physiologically unfavorably composed lacrimal fluid (dry-eye symptoms) can only be treated with tear substitutes at the moment. The cumbersome application thereof (eye drops several times a day) and their always poor effect have not yet achieved any genuine break-through when these symptoms are treated. Damage caused by chemical or physical action, such as acid burns or burns, continue to pose serious therapeutical problems. A genuine treatment which is conducive to the regeneration of conjunctivas and epitheliums is not available at the moment. Many people cannot wear contact lenses because their eyes will not accept such a foreign body. When suffering from one of the following symptoms, they will not be in a position to wear contact lenses as vision aids at any rate: keratoconjunctivitis sicca or Sjogren's syndrome, disorders of the mucin layer (Stevens-Johnson syndrome, acid burns, vitamin A-vitaminosis and ocular pemphigoid) and reduced cornea sensibility. Furthermore, reduced lacrimal fluid (for instance after oral administration of antidepressants, antihistamines, diuretics or spasmolytics), chronic eye inflammations (blepharitis, conjunctivitis, etc.), and stay in low air humidity (for instance flying personnel) often lead to problems with contact lenses. Most of these causes can nowadays not be eliminated therapeutically to such a degree that contact lenses could be worn without problems for a long period of time. The grey cataract leading to blindness without surgical intervention could at least partly be avoided by administering high doses of vitamin C (800 mg a day) if the results obtained by experts at the Tufts University at Boston are confirmed (6). According to these results the antioxidative effect of vitamin C is responsible for inhibiting the lens oxidation caused by old age. Vitamin C amounts which are so high are, however, not tolerated by many people when administered orally. It would therefore be desirable to provide physiologically acceptable antioxidative substances in the immediate vicinity of the eye lens. At the moment, however, such a therapeutic agent does not exist.

Brief Summary Text (152):
As already described in sections I and II, the physiological liposomes of the invention have antiviral and antiallergic properties that suggest their use as an ophthalmic agent. In addition to these therapeutical approaches, there are above all regeneration-supporting (see section I, point 8) and protective abilities of physiological liposomes. The front part of the eye, above all the cornea and the neighboring conjunctivae are coated by a permanent liquid film. Apart from nutrients, salts and antimicrobial substances, this lacrimal fluid also contains substances which prevent rapid evaporation (e.g. lipids and mucins). The composition of the lacrimal fluid wetting the cornea and conjunctivae follows from the secretion of various glands, with the lacrimal gland secreting the main part of

the fluid. Alveolar sebaceous glands (Meibomian gland), aprocrine glands (Moll's glands), as well as small accessory tear glands (Krause's glands) are seated in the eyelid itself. The bradytropic cornea, specifically the front cornea epithelium (5-6 layers of non-cornified epitheliums), is nourished by the lacrimal fluid through diffusion. This explains the special sensitivity of the cornea to disorders of the lacrimal fluid. As proved in Example 4 with reference to a group of patients having dry-eye symptoms, physiological liposomes, when applied externally to the eyelid, can contribute to a normalization of the fluid layer wetting the cornea and conjunctivae in many cases. The liposomes presumably penetrate through the very thin, multilayered cornified pavement epithelium of the front side of the eyelid, thereby supplying the lid-bound glands with fluid, nutrients and secretable substances (lipids) which slow down the evaporation of the eye fluid. Furthermore, studies with test persons having conjunctivitis caused by allergen or virus and with ceratitis show that upon application of physiological liposomes on the eyelid the "sand grain sensation" will disappear within a few minutes and the symptoms will decline in most cases within a day upon repeated application.

Brief Summary Text (153):
Hence, physiological liposomes are suited for the prophylactic and therapeutic treatment of eye diseases of allergic or viral etilogy, for instance;

Brief Summary Text (164):
ophthalmia sympathica

Brief Summary Text (167):
dry-eye symptoms

Detailed Description Text (4):
About 420 PFU (plaque forming units) of a fresh isolate of herpes simplex type 1 (1.2 ml) were incubated for different periods with a liposome suspension (1.2 ml) which contained 7.3.times.10.sup.13 liposomes per ml--unilamellar liposomes for the most part--after mixing. 3 g soybean lecithin were dissolved in 3 ml EtOH for preparing the liposomes. 3 g of sodium ascorbate, 0.27 g of common salt and 0.4 g of sodium cholate were dissolved in 23 ml double distilled water. The two solutions were well mixed by stirring, and the heterogenous mixture was sterilized by filtration at 5.times.10.sup.6 Pa. The resultant liposome dispersion was adjusted to pH 6.8 with 1N hydrochloric acid and diluted to the necessary test concentrations. The virus-liposome mixture was then added to a confluent monolayer of monkey kidney cells of the vero type for 15 minutes and subsequently replaced by medium. The evaluation of the PFU created by the lytic viruses was done after 72 hours. The results of the tests are shown in FIGS. 1a and 1b. The control was applied for time 0, i.e., viruses were added to the cells without liposomes. 420 PFU were measured after 3 days, which was equated with 100% PFU in the Fig. When the viruses were pipetted together with the liposomes and then immediately given to the cells, one only found 47% of the PFU in comparison with the control. This period of interaction of the liposomes with the viruses is about half a minute. After an incubation of the viruses with the liposomes for 10 minutes, only 26% PFU remained while less than 1% of the PFU could be detected after 30 minutes. About half of the viruses are directly inactivated after contact with the liposomes while some viruses remain infectious in the liposome suspension up to 30 minutes. This could be due to the heterogeneous morphology of the virus envelopes.

Detailed Description Text (13):
On the basis of the almost complete inhibition of the herpes viruses in a liposome concentration of from 7.3.times.10.sup.13 /ml (Experiment 1) and the rapid decrease in inhibition in the case of slightly lower liposome concentrations (Experiment 2), there follows a relationship from the packing density of the liposomes and the size of the herpes viruses (diameter between 120 and 200 nm), which shall be shown in the following by way of a model:

Detailed Description Text (39):
In accordance with the present results, the most effective liposome concentration might be at about 7.times.10.sup.13 liposomes/ml, depending on the incubation period and virus concentration. As for the calculated spacings, the model does not consider the interactions in the direct vicinity of the liposomes and viruses (hydrate envelopes, ion deposition, etc.) which might lead to an increase in spacing and thus to a lower effective liposome concentration. Moreover, since the forces are unknown which permit an interaction (fusion) of liposomes and herpes viruses after all, no definite information can be furnished about the model. If fusogenic proteins play no catalytic role in the interaction of liposomes and herpes viruses, one can assume that both particles must approach each other up to about 1.5 nm under displacement of the water molecule to permit a fusion. This is an energetically highly unfavorable process (12). This might only take place at a liposome density as is here the case. The good correspondence between the theoretical average value of 6.4.times.10.sup.13 and the detected liposome concentration of 7.3.times.10.sup.13 /ml with an effect of almost 100% is here striking, as well as the correspondence of the rapid decrease in virus inhibition, which decrease can be forecast by the model, with the measured values at even slightly lower liposome concentrations. With a topic treatment of herpes patients, liposome concentrations of about 7.times.10.sup.13 /ml have turned out to be effective. An at least partial protection of the cells can also be achieved with lower liposome concentrations, as shown in Experiment 2.

Detailed Description Text (48):
Physiological liposomes for treating dry-eye symptoms

Detailed Description Text (49):
Twenty patients with dry-eye symptoms were treated with physiological liposomes over a period of 4 months. 12 patients then appeared for control tests. The subjective assessment by the patients was as follows:

Current US Original Classification (1):
424/450

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L9: Entry 2 of 2 File: USPT May 28, 2002

DOCUMENT-IDENTIFIER: US 6395294 B1
TITLE: Method of visualization of the vitreous during vitrectomy

Abstract Text (1):
A composition for rendering a vitreous cavity visible during a surgical procedure to alleviate a structural disorder caused by the vitreous in an eye, and a method of using the composition. The composition is a vitreous delineating agent that is translucent, opaque or semi-opaque and is in a formulation that may be a solution, a suspension or an emulsion. The agent may be a liposome or microsphere that may additionally contain a therapeutic agent. In use, the agent marks or delineates the vitreous cavity, allowing a surgeon to clearly visualize the entire cavity. Use of the method improves accuracy of a vitrectomy and thus prevents suboptimal outcomes or the need for repeated procedures.

Brief Summary Text (6):
A patient suffering from any of these conditions may undergo a surgical procedure, such as pars plana vitrectomy, in an attempt to alleviate these conditions. However, the surgical procedure itself also produces complications. Postoperative intraocular fibrin formation is a common complication of vitrectomy surgery and penetrating ocular injury. Extensive intraocular surgery, epiretinal membrane dissection in proliferative vitreoretinopathy, and inflammatory conditions such as endophthalmitis and uveitis exaggerate postoperative intraocular fibrin formation because of increased vascular permeability. Additional surgical procedures such as endophotocoagulation, cryopexy, scleral buckling, and intraocular gas introduction also exacerbate the intraocular inflammation. Various other factors have been implicated in fibrin formation including a preoperative retinal detachment, combined surgery (lensectomy and vitrectomy), and severe or prolonged hypotony. Eyes with proliferative diabetic retinopathy are especially susceptible to fibrin formation because long-term disease damages the blood retinal barrier. Laser and cryopexy have been shown experimentally to compromise the blood retinal barrier, enhancing the ability of the vitreous to stimulate retinal pigment epithelium migration and proliferation, thereby increasing the incidence of tractional retinal detachment. Additionally, a high percentage of surgeries fail in severely diseased, previously operated, and uveitic eyes, and effective treatment of retinal detachment with a proliferative vitreoretinopathy component, severe proliferative diabetic retinopathy with traction retinal detachment, and persistent ocular inflammatory disease remain a challenge for vitreoretinal specialists.

Brief Summary Text (10):
The invention is directed to a method to alleviate a structural disorder of an eye. A vitreous delineating agent is injected into the eye in an effective amount to allow the vitreous to be visible to a surgeon, enabling the surgeon to alleviate the disorder. The agent may be a therapeutic agent, an inert agent, or an inert agent that contains a therapeutic agent, such as a microsphere or liposome containing a therapeutic agent. In one embodiment the agent is a corticosteroid but may be, for example, an antiinfective agent, an immunosuppressant agent, an antiproliferative agent, and/or an antiangiogenesis agent. The agent may be in a formulation such as a solution, an emulsion, or a suspension.

Brief Summary Text (11):
The invention is also directed to a method to alleviate a structural disorder of an eye by injecting a corticosteroid formulation into the eye in an effective amount to enable a surgeon to visualize the vitreous and to thus alleviate the disorder. The corticosteroid formulation may also contain an additional therapeutic agent, and/or may be incorporated into a vesicle such as a microsphere or a liposome.

Detailed Description Text (3):
The agent must be visible to the surgeon during surgery; that is, the agent must itself be translucent (transmitting light but causing sufficient diffusion to eliminate perception of distinct images), opaque (impenetrable by light), or semi-opaque (partially impenetrable by light), or be rendered translucent, opaque or semi-opaque. Visualization may be with the naked eye or with the assistance of instrumentation such as an operating microscope. The agent may be a therapeutic agent such as an anti-inflammatory agent, antimicrobial agent, anti-angiogenesis agent, or antiproliferative agent, or an inert substance such as a blank microsphere or liposome, or combinations of the above (for example, a microsphere or liposome containing any of the above therapeutic agents), as long as they are visible during the surgical procedure. A combination of agents may be used.

Detailed Description Text (10):
In other embodiments of the method, the agents may be incorporated into vesicles which provide a translucent, semi-opaque or opaque injectable. Examples of such vesicles include liposomes or microspheres, for example, poly(glycolic) or poly (lactic) acid microspheres. Incorporation of agents into liposomes or microspheres may be performed by routine procedures as known to one skilled in the art.

Current US Cross Reference Classification (3):
424/450

CLAIMS:

3. The method of claim 1 wherein said agent is formulated as a vesicle selected from the group consisting of a liposome and a microsphere.

7. The method of claim 6 wherein the corticosteroid is incorporated in a vesicle selected from the group consisting of a microsphere and a liposome.

12. The composition of claim 8 wherein said agent is a vesicle selected from the group consisting of a liposome and a microsphere.

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Refine Search

Search Results -

Terms	Documents
L8 and (424/450).ccls.	2

Database: US Pre-Grant Publication Full-Text Database; US Patents Full-Text Database; US OCR Full-Text Database; EPO Abstracts Database; JPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Search: L9

Refine Search | Recall Text | Clear | Interrupt

Search History

DATE: Thursday, April 19, 2007 **Purge Queries** Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L9	L8 and 424/450.ccls.	2	L9
L8	(endophthalmitis) and liposome	409	L8
L7	(endophthalmitis) same liposome	1	L7
L6	(endophthalmitis) adj10 liposome	0	L6
L5	L4 and 424/450.ccls.	3	L5
L4	L3 and (eye or ophthalm$)	131	L4
L3	(herpes) adj10 liposome	526	L3
L2	(herpes adj1 ophthalmicus)	3	L2
L1	liposome same (herpes adj1 ophthalmicus)	0	L1

END OF SEARCH HISTORY

L5: Entry 3 of 3 File: USPT Dec 29, 1998

DOCUMENT-IDENTIFIER: US 5853753 A
** See image for Certificate of Correction **
TITLE: Liposomes, method of preparing the same and use thereof in the preparation of drugs

Brief Summary Text (50):
Furthermore, it has been found that a drug containing the liposomes according to the invention is well suited for treating dental neck sensitivity. Another possible use is the use of the inventive liposomes for the prophylactic and/or therapeutic treatment of allergically and/or virally caused eye inflammations. Furthermore, the liposomes of the invention can be used on the eye for the prophylactic and/or therapeutic treatment of the dry-eye symptom.

Brief Summary Text (109):
Internal and external means are available for treating such allergies. As a rule, skin allergies are treated with the aid of external means; in serious cases internal means are additionally administered. Since the cause of a resulting skin allergy is often not known, a reliable diagnosis is made very difficult. As a consequence, so-called "harmless" antiallergics are used for treatment at the initial stage, which agents often just alleviate the complaints or do not show an effect at all. A physician is therefore forced to continue his/her treatment and to resort to dermatics, antibiotics and antimycotics (with secondary infections allergy-damaged skin parts), i.e., to drugs which contain chloramphenicol, rifampicin, flumethasone, dexamethasone, triamincinolonacetonide or hydrocortisone, just to mention a few. Many of these "hard" drugs have limited uses and may, in turn, cause side effects, such as skin atrophy, steroid acne, etc. Dermatologists fear, e.g., the rebound effect after the administration of cortisone has been discontinued. Furthermore, they often dry the skin and must not be brought into contact with the eye conjunctiva (see section IV). A problem which is found in the administration of external antiallergics is insufficient absorption through the skin. Penetration of the drugs is rendered especially difficult if these are water-soluble. A comparable problem arises when the active substance is lipophil and must be applied in the form of a crystalline suspension. The effectivity of external antiallergics is therefore considered to be unsatisfactory.

Brief Summary Text (125):
Physiological liposomes are excellently suited for controlling skin or mucous membrane allergies. The term mucous membrane allergy predominantly covers allergic reactions of the nasal, buccal or ophthalmic mucous membrane which are triggered by contact with corresponding allergens. The immunological mechanisms which take place here are similar to those of the skin allergies discussed hereinafter with reference to the earring allergy. The term skin allergy covers syndromes of different geneses of which all, however, lead to a similar, more or less locally defined skin reaction (allergy).

Brief Summary Text (149):
IV. Use of physiological liposomes of the invention for the prophylactic and therapeutic treatment of eye diseases

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Search Results -

Terms	Documents
L3 and (eye or ophthalm$)	16

Database:
US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
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IBM Technical Disclosure Bulletins

Search: L4

Refine Search | Recall Text | Clear | Interrupt

Search History

DATE: Thursday, April 19, 2007 **Purge Queries** Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L4	L3 and (eye or ophthalm$)	16	L4
L3	liposome same diclofenac	55	L3
L2	liposome adj15 diclofenac	6	L2
L1	liposome adj10 diclofenac	6	L1

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L1: Entry 6 of 6 File: USPT Feb 10, 1998

DOCUMENT-IDENTIFIER: US 5716638 A
TITLE: Composition for applying active substances to or through the skin

Brief Summary Text (105):
The following experimental results, relate to various liposome systems of the invention containing 1% sodium diclofenac as model drug and in which various compositional factors have been changed: 1. the concentration of alcohol 2. the phospholipid 3. the type of alcohol. The results demonstrate: 1. the cruciality of high concentrations of alcohol, and that the high skin permeation from ethosomal systems of the invention is still obtained: 2. with an additional example of phospholipid (Lipold E 75-containing phosphatidyl ethanolamine and phosphatidyl choline isolated from egg, produced by Lipold KG; Germany, 3, with isopropyl alcohol,

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L4: Entry 9 of 16 File: PGPB Jun 28, 2001

PGPUB-DOCUMENT-NUMBER: 20010005501
PGPUB-FILING-TYPE: new-utility
DOCUMENT-IDENTIFIER: US 20010005501 A1

TITLE: HYALURONIC DRUG DELIVERY SYSTEM

PUBLICATION-DATE: June 28, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
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US-CL-CURRENT: 424/1.21; 424/282.1, 424/401, 424/450, 424/458, 424/85.1

CLAIMS:

1. A pharmaceutical composition comprising: a mixture of hyaluronic acid and liposomes with the proviso that said composition does not contain superoxide dismutase (SOD).

2. The pharmaceutical composition according to claim 1, wherein said composition further comprises a pharmaceutically active substance encapsulated in said liposomes.

3. The pharmaceutical composition according to claim 2, wherein said pharmaceutically active substance is hydrophobic.

4. The pharmaceutical composition according to claim 2, wherein said pharmaceutically active substance is cyclosporin A.

5. The pharmaceutical composition according to claim 1, wherein said liposome is multilamellar.

6. The pharmaceutical composition according to claim 1, wherein said hyaluronic acid has an average molecular weight of 10,000 to 1,000,000 daltons.

7. The pharmaceutical composition according to claim 1, wherein said liposomes are negatively charged.

8. The pharmaceutical composition according to claim 1, wherein said liposomes have an average maximum diameter in the range of 80 to 1040 nanometers.

9. The pharmaceutical composition according to claim 8, wherein said liposomes have an average maximum diameter in the range of 200 to 900 nanometers.

10. The pharmaceutical composition according to claim 4, wherein said pharmaceutical composition contains 13.165% by weight liposomes, 2.5% hyaluronic acid, and 13.5 milligrams cyclosporin A per gram liposomes.

11. A composition according to any of claims 1 to 10 comprising a selected polynucleotide for gene therapy.

12. A composition according to claim 11 wherein the selected polynucleotide is located within the liposomes.

13. A composition according to claim 11 or claim 12 wherein the selected polynucleotide comprises a plasmid or vector which is capable of transfecting target somatic cells.

14. A method for preparing a pharmaceutical composition having hyaluronic acid and liposomes, said method comprising; producing liposomes from phospholipids; mixing said liposomes with said hyaluronic acid.

15. The method according to claim 14, said method further comprising: conducting said liposome production in the presence of a pharmaceutically active substance.

16. The method according to claim 15, wherein said pharmaceutically active substance is cyclosporin A.

17. The method according to claim 16, wherein said pharmaceutical composition contains 13.2% by weight liposomes, 2.5% by weight hyaluronic acid, and 13.5 milligrams cyclosporin A per gram liposomes.

18. A method according to claim 14 or claim 15 wherein the pharmaceutically active substance is a selected polynucleotide for gene therapy.

19. A method according to claim 18 wherein said liposome production is conducted in the presence of said selected polynucleotide wherein in the produced liposomes, the polynucleotide is located within the liposomes.

20. A method for treating an animal, having a disease capable of being treated with a pharmaceutical composition including hyaluronic acid liposomes and a therapeutically effective amount of a pharmaceutically active substance, said method comprising administering said pharmaceutical composition to the animal with the proviso that said composition does not contain superoxide dismutase (SOD).

21. A method according to claim 20, wherein said pharmaceutical composition is administered orally.

22. A method according to claim 20 wherein said pharmaceutical composition is administered parenterally.

23. A method according to claim 20, wherein said pharmaceutical composition is administered intrarectally.

24. A method according to claim 20, wherein said pharmaceutical composition is administered to the lungs.

25. A method according to claim 20, wherein said pharmaceutical composition is administered to the eyes.

26. A method according to any of claims 20 to 25, wherein said pharmaceutically active substance is cyclosporin A.

27. A method according to claim 26, wherein said cyclosporin A is present in said pharmaceutical composition in an amount of 13.5 milligrams per gram liposomes.

28. A method according to any of claims 20 to 25, wherein said pharmaceutically active substance is a polynucleotide for gene therapy.

29. A method of gene therapy which comprises administering a selected polynucleotide to an animal having a disease treatable by gene therapy, said polynucleotide being administered in the form of a composition comprising hyaluronic acid.

30. A method according to claim 29, wherein said composition additionally comprises liposomes.

31. A method according to claim 29, wherein the polynucleotide is contained within the liposomes.

32. The use of hyaluronic acid in the manufacture of a pharmaceutical composition for use in gene therapy.

33. The use according to claim 32, wherein the pharmaceutical composition includes liposomes.

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L4: Entry 15 of 16 File: USPT Oct 18, 1994

DOCUMENT-IDENTIFIER: US 5356633 A
TITLE: Method of treatment of inflamed tissues

Detailed Description Text (72):
Other agents generally useful in the treatment of inflammation include, but are not limited to free radical scavenging agents such as superoxide dismutase and nonsteroidal antiinflammatory drugs (NSAIDs), including, but not limited to salicylates (exemplified by aspirin), pyrazolon derivatives (exemplified by phenylbutazone), indomethacin, sulindac, tolmetin, fenamates (exemplified by meclofenamate), proprionic acid derivatives (exemplified by ibuprofen), oxicam derivatives (exemplified by piroxicam), phenylacetic acid derivatives (exemplified by diclofenac), etodolac, and nabumetone. Generally, although many of these drugs possess excellent antiinflammatory properties, side effects limit their use at doses effective to provide effective antiinflammatory treatment. In accordance with the invention, formulations of such drugs in liposomes having enhanced circulation times will are contemplated to provide selective relief of inflammation in subjects requiring such treatment. Other exemplary antiinflammatory agents are discussed with respect to specific indications, below.

Detailed Description Text (78):
Neurogenic inflammation refers to a local tissue response elicited by stimulation of sensory nerves in a number of tissues. Commonly, susceptible organs include the eye, skin, joints and respiratory tract. In animal models of the respiratory tract, neurogenic inflammation is characterized by increased permeability of postcapillary venules and collecting venules in specific regions of the respiratory tract (McDonald). Systemic antiinflammatory therapy using the liposomal preparations of the invention is therefore expected to be useful in the delivery of therapeutic agents useful in the treatment of neurogenic inflammation.